REMARKS

Claims 1-9 and 14-19 are, subject to entry of this amendment, pending and under consideration. Claims 10-13 and 21-25 have been withdrawn from consideration via Applicants' previous election without traverse of Group I in response to the Restriction Requirement issued on June 18, 2002. Claims 1-5, 8, 9, 14-16, and 19 are amended as described herein. Claims 10-13 and 21-25 are cancelled without prejudice to the prosecution of their subject matter in other patent applications. Claim 20 is cancelled as redundant over amended claims.

Claims 1, 3, 4, 6-9, 14 and 16-20 are rejected under the first paragraph of 35 U.S.C. § 112 as failing to satisfy the written description requirement. Claims 1, 3, 5-9, 15, 16 and 20 are rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite. Claims 1, 3, 6-9, 14 and 17-20 are rejected under 35 U.S.C. § 103(a) as being obvious over El-Deiry *et al.*, Cell 1993;75:817-825 (hereinafter "El-Deiry") in view of Jiang *et al.*, Oncogene 1995;10:1855-1864 (hereinafter "Jiang"). The Examiner also has objected to the specification and Figure 6 on the basis of certain informalities detailed below.

In accordance with the Revised Amendment Format published as a "Pre-OG Notice" by the Office of Patent Legal Administration, wherein the provisions of 37 C.F.R. § 1.121(a), (b), (c), and (d) are waived for amendments to the claims, specification and drawings in all applications in all Technology Centers provided that the amendments comply with the revised amendment format, Applicants herein provide an amendment in the revised format in which (1) each of the sections detailing the amendments to the specification, amendments to the claims, amendments to the drawings, and remarks begins on a separate sheet, 2) a complete listing of all claims in ascending order with proper status identifiers is presented in each amendment wherein claims are being added,

deleted or amended, 3) amendments to the specification are made by presenting replacement paragraphs marked up to show changes, and 4) amendments of drawings are made by submission of unmarked replacement drawings.

For reasons set forth below, Applicants respectfully request that the rejections be removed and the claims be allowed to issue.

I. The Drawings are Correctly Labeled

The drawings are objected to because Figure 6 refers to a nucleotide at position 0. In response, Applicants submit herewith a replacement Figure 6, wherein the positions of the nucleotides within the sequence of SEQ ID NO:1 have been amended to remove negative positions and position 0, bringing the positions of the nucleotides contained within this figure in accordance with the numbering scheme of SEQ ID NO:1. Applicants respectfully request that the Examiner now remove the objection to the drawings.

II. The Specification Correctly References SEQ ID NO:1

The text of the specification at page 10, line 21, and page 13, lines 29-33 are objected to as incorrectly referencing the positions of certain nucleotides of the *mda*-7 promoter relative to the sequence of SEQ ID NO:1.

In response, Applicants have amended the specification as indicated herein to bring the numbering system employed to refer to specific nucleotides within the *mda*-7 promoter into accordance with the numbering scheme of SEQ ID NO:1. Specifically, Applicants have amended the text of the specification on page 10, lines 19-21, on page 11, lines 22-24, on page 11, lines 26-29, on page 13, lines 29-33, on page 14, line 3, and on page 15, line 16 as indicated hereinabove. In light of these changes, Applicants respectfully request that the Examiner remove the objection to the

specification.

III. The Claims Are Drawn to the Elected Invention

Claims 8, 9, and 14-19 are objected to as encompassing more than the elected invention. According to the Examiner, the claims as originally worded could be read on non-elected *in vivo* applications in addition to the elected *in vitro* applications because they refer to a "host cell" rather than an "isolated host cell".

In response, Applicants have amended Claims 8, 9, and 14-16 to specify that the "host cell" is an "isolated host cell" (Claims 8, 9 and 14) and to delete the phrase "topical application to the cell" from Claim 19. Applicants assert that the claims as presently amended are properly limited to the scope of the elected invention and respectfully request that the Examiner withdraw the objection to Claims 8, 9 and 14-19.

IV. The Claims Are Definite

Claims 1, 3, 5-9, 15, 16 and 20 are rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 5, 15, 16 and 20 are held by the Examiner to be indefinite for reciting negative nucleotide positions in the nucleotide sequence of SEQ ID NO:1, which has no negative sequence positions.

In response, Applicants have amended Claims 5, 15, 16 and 20 to correctly recite the positions of certain nucleotides of the *mda*-7 promoter relative to the sequence of SEQ ID NO:1.

Claims 1, 20 and the claims dependent therefrom are held by the Examiner to be indefinite

for employing the term "stringent conditions," which the Examiner maintains is not adequately defined in the specification.

Claims 1, 16 and 20 are held by the Examiner to be indefinite for inclusion of the term "functionally equivalent." The Examiner asserts that, although the term "functionally equivalent" is defined in the specification, *see* page 16, lines 1-8, the definition is not satisfactory because it includes the phrase "substantially similar" when referring to the unique characteristics of the *mda*-7 promoter that necessarily would be present in other promoters that are functionally equivalent to the *mda*-7 promoter. The Examiner further asserts that the specification does not provide any concrete limitations that are covered by the phrase.

In response, Applicants first assert that "stringent conditions" for hybridization are known in the art. Because the specification need not teach what is known in the art, this term need not be expressly defined. However, in order to advance the prosecution of this application and without prejudice, Claims 1-5, 14, 15 and 20 are amended to no longer refer to nucleic acid molecules that are "functionally equivalent" to SEQ ID NO:1 or that hybridize to a sequence complementary to SEQ ID NO:1 in hybridizations performed under "stringent conditions." Instead, the claims are directed toward isolated nucleic acid molecules that are at least about 80% identical to the core promoter sequence of SEQ ID NO:1 and that possess certain specific functional characteristics. Support for these amendments may be found on p. 15, lines 22-25 of the specification, and on p. 66, lines 10-26. Applicants believe that the amended claims more particularly define the metes and bounds of the subject matter that Applicants regard as their invention and are therefore definite. In light of these amendments, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1, 3, 5-9, 16 and 20 under the second paragraph of 35 U.S.C. § 112.

IV. The Claims Satisfy the Written Description Requirement of 35 U.S.C. § 112, first paragraph

Claims 1, 3, 4, 6-9, 14 and 16-20 are rejected under the written description requirement of the first paragraph of 35 U.S.C. § 112 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that there is insufficient written description for the *mda*-7 promoter to support claims drawn toward nucleotide sequences that are functionally equivalent to the *mda*-7 promoter of SEQ ID NO:1 or to nucleotide sequences that hybridize to this same sequence under stringent conditions.

Applicants respectfully traverse this rejection. However, in the interest of furthering the prosecution of this case and to bring greater clarity to the claims, Applicants have amended Claims 1-5, 14, 15 and 20. As amended, Claims 1-5, 14, 15 and 20 are directed toward isolated nucleic acid molecules that are at least about 80% identical to the core promoter sequence of SEQ ID NO:1 and that possess certain functional characteristics. The specification provides ample support for molecules with these functional and structural features. For example, Figure 1 demonstrates that the *mda*-7 promoter is active and inducible in both HO-1 and MeWo melanoma cells.

Similarly, the specification precisely defines the nucleic acid sequence of one embodiment of the *mda*-7 promoter (SEQ ID NO:1), and indicates that other embodiments of the promoter would include those molecules with substantial homology to the *mda*-7 sequence of SEQ ID NO:7, provided that they retain the critical functional characteristics of the *mda*-7 promoter as detailed immediately above, and wherein substantial homology is defined on page 15 of the specification as at least about 80% identity over a defined length of the molecule.

Combining these functional and structural data, Applicants contend that the specification provides adequate written description of the invention as presently claimed so as to convey to an artisan of ordinary skill that Applicants were in possession of the claimed invention at the time that the application was filed. Applicants therefore respectfully request that the Examiner withdraw the rejection of Claims 1, 3, 4, 6-9, and 16-20 under the first paragraph of 35 U.S.C. § 112.

VIII. The Invention Is Not Obvious

Claims 1, 3, 6-9, 14 and 17-20 are rejected under 35 U.S.C. § 103(a) as being rendered obvious by El-Deiry *et al.*, Cell 1993;75:817-825 (hereinafter "El-Deiry") in view of Jiang *et al.*, Oncogene 1995;10:1855-1864 (hereinafter "Jiang"). According to the Examiner, Jiang teaches that *mda*-6 is identical to WAF1, which encodes the p21 protein, and that the p21 gene is differentially expressed in melanoma cells. Since expression of the endogenous p21 gene is presumably controlled by the p21 promoter, the p21 promoter would qualify as a promoter that is functionally equivalent to the *mda*-7 promoter of the instant invention, because, as shown in Figure 4 of the instant application, the activity of the WAF1/p21/*mda*-6 promoter is regulated in a substantially similar to that of the *mda*-7 promoter. El-Diery teaches the use of a WAF1 (p21/*mda*-6) promoter to drive the expression of the heterologous coding sequence for luciferase. Thus, the Examiner contends that the combined teachings of Jiang and El-Deiry produce a WAF1/p21/*mda*-6 promoter that displays regulatory behavior that is "substantially similar" to the *mda*-7 promoter and that has been used to drive the expression of a heterologous gene. According to the Examiner, this combination of teachings satisfies all of the limitations of Claims 1, 3, 6-9, 14 and 17-20 and therefore renders obvious the instant invention.

In response, Applicants note that, as amended, Claims 1, 3, 6-9, 14 and 17-20 no longer recite

the "substantially similar" language that the Examiner contends could read on the *mda*-6 promoter. The amended claims now are directed toward isolated nucleic acid molecules that are at least about 80% identical to the core promoter sequence of SEQ ID NO:1 and that possess certain functional characteristics such as activity in melanoma cells and induction by differentiation inducers. Applicants contend that, while the *mda*-6 arguably may be active in melanoma cells and induced during differentiation, the *mda*-6 promoter is not 80% identical to the sequence of SEQ ID NO:1. Thus, the teaching of El-Deiry, either alone or in combination with Jiang, does not render obvious Claims 1, 3, 6-9, 14 and 17-20 of the instant invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1, 3, 6-9, 14 and 17-20 under 35 U.S.C. § 103(a).

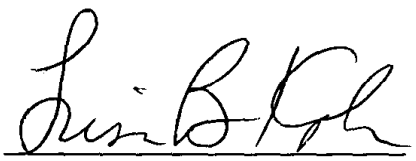
CONCLUSION

Based on the foregoing remarks and in light of the amendments, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Applicants believe a fee of $465.00 is due with this response for a three-month extension of time as required under 37 C.F.R. §1.17(a)(3). Should any additional fees be required, the Commissioner is hereby authorized to charge Deposit Account Number 02-4377. A duplicate copy of this communication is enclosed.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

Respectfully submitted,



Lisa B. Kole
Patent Office Reg. No. 35,225

Attorney for Applicants
(212) 408-2628

Enclosures